Turk J Intensive Care 2023;21:239-47
DOI: 10.4274/tybd.galenos.2022.94834

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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The Evaluation of Nosocomial Candidemia in Pediatric Intensive Care: A Single-center Study

Çocuk Yoğun Bakımda Nozokomiyal Kandideminin Değerlendirilmesi: Tek Merkez Çalışması

Received/Geliş Tarihi : 29.05.2022
Accepted/Kabul Tarihi : 17.11.2022

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ABSTRACT *Objective:* Patients in pediatric intensive care units are more likely to develop serious nosocomial infections due to comorbidities, longer and more invasive procedural treatments, and the development of immunosuppression. We described *Candida* infections, management, morbidity and mortality in critically ill pediatric patients.

Materials and Methods: A retrospective single-center study includes patients aged 1 month-18 years treated against candidemia from January to December 2021. This included those who had blood cultures of *Candida* species growth. We excluded patients with infection *Candida* in endotracheal aspiration and/or urinary specimens, etc. The demographic characteristics, medical histories, comorbidities, length of stay, need for mechanical ventilation supports, laboratories, relationship use of catheters and total parenteral nutrition, treatment periods, antifungal response/resistance, duration of treatment and adverse effects, morbidities/mortalities.

Results: In this study, the total mortality rate was 40.7%, and the mortality rate due to candidemia was detected at 44.4%, but the correlation between candidemia and mortality was not significant (p=0.975). However, 18.5% of them are caused by nosocomial. The mortality risk did not change for subtypes (p=0.975). No significant correlation was found when mortality (p=0.07) and central venous catheter infection (p=0.563) were compared using total parenteral nutrition.

Conclusion: In our study, in which 27 patients were followed up for nosocomial candidemia, the rate of candidemia was found to be higher in patients with comorbidity, long-term mechanical ventilation support, central venous catheter use, long hospital stay, parenteral nutritional support, and high Pediatric Risk of Mortality III score. *C. parapsilosis* was detected most frequently in our *Candida* subtype unit with a rate of 59.3%. The fluconazole 8 (29.6%), amphotericin B 18 (66.7%) and voriconazole 1 (3.7%) patients were initiated. At this treatment time, only 4 (14.8%) patients developed organ failure. In our study, we detected a total mortality rate of 40.7%. However, 18.5% of them were caused by nosocomial candidemia. Considering all these reasons, we believe that our risk factors, diagnosis, treatment, follow-up, and management process will contribute to the literature.

Keywords: Pediatrics, intensive care unit, nosocomial, candidemia

ÖZ *Amaç:* Çocuk yoğun bakımdaki hastaların komorbiditeleri, daha uzun ve invaziv prosedürel tedavilerin olması ve immünosüpresyon gelişimi nedeniyle ciddi nozokomiyal enfeksiyonların gelişme olasılığı daha yüksektir. Çalışmamızda, üçüncü basamak hastanemizde kritik pediatrik hastalarda kan kültüründe *Candida* saptanan hastaların izlem süreci, morbidite ve mortalitesini tanımlamayı amaçladık.

Gereç ve Yöntem: Retrospektif tek merkezli çalışmamızda, Ocak 2021-Aralık 2021 döneminde ünitemizde yatan 1 ay-18 yaş arası ve kan kültüründe *Candida* türleri üremesi olanlar dahil edilmiştir. Sadece endotrakeal aspirasyon ve/veya idrar örneklerinde *Candida* türleri enfeksiyonu üremesi olan hastalar çalışma dışı bırakılmıştır. Çalışmamızda hastaların demografik özellikleri, tıbbi öyküsü, komorbiditeleri, hastane yatış süresi, mekanik ventilasyon ihtiyacı, laboratuvar değerleri, kateter kullanımı ve total parenteral beslenme ile ilişkisi, tedavi süreleri, antifungal tedaviye yanıt/direnç durumu ve yan etkiler morbidite/mortalite durumu incelenmiştir.

Bulgular: Çalışmamızda toplam ölüm oranı %40,7, kandidemiye bağlı ölüm oranı %44,4 olarak saptandı, ancak kandidemi ile ölüm arasındaki ilişki anlamlı değildi (p=0,975). Bunların %18,5'inin nozokomiyal kandidemiden kaynaklandığı görüldü. Mortalite riski, kandida türleri arasında farklılık göstermemektedir (p=0,975). Parenteral beslenme kullanılmasının mortalite (p=0,07) ve santral venöz kateter enfeksiyonu (p=0,563) ile anlamlı bir ilişkisi saptanmamıştır.

Sonuç: Hastane kaynaklı kandidemi nedeniyle 27 hastanın takip edildiği çalışmamızda komorbidite, uzun süreli mekanik ventilasyon desteği, santral venöz kateter kullanımı, hastanede uzun süre kalma, parenteral beslenme desteği ve yüksek Pediatrik Ölüm Riski III puanı olanlarda daha yüksek oranda bulunmaktadır. *C. parapsilosis* en sık *Candida* alt tipi olarak ünitemizde %59,3 ile tespit edildi. Hastalara flukonazol 8 (%29,6), amfoterisin B 18 (%66,7) ve vorikonazol 1 (%3,7) başlanmıştı ve bu tedavi süresinde hastaların sadece 4'ünde (%14,8) organ yetmezliği gelişmiştir. Çalışmamızda toplam mortalite oranı %40,7 olarak tespit edildi. Öte yandan, bu ölümlerin %18,5'i hastane kaynaklı kandidemiden kaynaklanmıştır. Tüm bu nedenlerle kandidemi risk faktörleri, tanısı, tedavi, izlem ve yönetim sürecimizin literatüre katkıda bulunacağı düşüncesindeyiz.
Anahtar Kelimeler: Pediatri, yoğun bakım ünitesi, nozokomiyal, kandidemi

Introduction

In hospitalized children bloodstream infections after bacterias and viruses, *Candida* represents the third most common cause (1). In children, nosocomial candidemia is one of the most frequent reasons of healthcare-associated infections (2). The most encountered etiology of *Candida* infections is the increased length of hospital stay, and the most severe conclusions are associated with increased morbidity and mortality (3). Intensive care unit (ICU) stay, is a strong risk factor that is having *Candida* species bloodstream infections. Especially in the pediatric age group having comorbidity, longer and invasive procedural treatment and immune system malfunction more likely to occur these infections in the pediatric intensive care unit (PICU) (4,5). Using of central venous (CVC) and arterial catheters (AVC), intravenous parenteral nutrition, increased length of ICU stay, previous broad-spectrum and prolonged antibiotics, immunodeficiency, cancers, bone marrow transplantation, endotracheal intubation and colonization with *Candida* spp. are reported to increase nosocomial *Candida* infections (6). Candidemias are a kind of life-threatening infection for immunocompromised patients. Although the risk factors for candidemia in critically ill children are known, it is necessary to treat with central lines (CVC, AVC, etc.), total parenteral nutrition (TPN), broad-spectrum antibiotics, and increased length of stay. In all pediatric populations (not only in PICU) the candidemia incidence was reported in various studies as 0.21-10.5 cases/1000 admissions (7). The type of candidemia, management and outcome have different among the study centers. The reason for this links closely to differences in different countries local prevention, prophylaxis and treatment practices. Currently, the lack of guidelines for candidemia management in PICU is caused to be different results in management and treatment (8). In this single-center retrospective study, we aimed to describe *Candida* infections, management, morbidity, mortality in critically pediatric patients and evaluate the risk factors and effects of nosocomial candidiasis in a tertiary level hospital in PICU.

Materials and Methods

We performed that a retrospective, single-center study which including patients ages 1 month-18 years treated against candidemia the periods from January to December 2021 in PICU. Our hospital is an 800-bed 3rd level hospital and the PICU is a 52-bed unit in which annual admission is about 1400 patients a year. In this heterogeneous population of admissions (pneumonia, sepsis, trauma, metabolic diseases, status epilepticus, genetic disorders, etc.), at the time of stay in PICU, we evaluated their all infections. In this study, we included the patients, all the year 2021 who had blood and/or CVC blood cultures *Candida* species growth. We excluded patients with infection of *Candida* species in only one area a pulmonary, urinary, abdomen, thorax, extremities, etc. because of not being invasive *Candida* infections. Additionally, if the patient's age is from 1 month-18 years, they were excluded from the study, too.

The demographic characteristics, medical histories, comorbidities, length of stay in PICU, need for mechanical ventilation supports, laboratories, relationship with the use of catheters and TPN, treatment periods, antifungal treatment response/resistance, duration of treatment and adverse effects, morbidities, and mortalities of patients whose electronic and archive files were examined and evaluated.

The Pediatric Risk of Mortality III (PRISM III) score, which is one of the most commonly used mortality detection scoring systems in PICUs, was used when examining patient data. While calculating the PRISM III score, 17 different parameters including the patient's vital signs, mental status, pupillary reflex, blood gas measurements and biochemical values in the first 24 hours are used. High scores indicate a high risk of mortality.

In our study, in a patient hospitalized in PICU for treatment due to any disease; nosocomial candidemia was defined as the presence of *Candida* growth in the blood culture that developed at least 48 hours after hospitalization, disrupted the patient's clinical condition, and required new treatment.

In the presence of a CVC used in a patient, if there was no other focus of infection, isolation of the same *Candida* species in the blood culture taken from the CVC at the same time as the peripheral blood, additionally as the growth in the catheter blood in a shorter time than in the vein blood was catheter-related blood flow was defined as infection.

The definition of resistance to fluconazole, in culture identification and sensitization form were evaluated in microbiology. In addition, the condition of fluconazole resistance was considered to be non-decreased in infection markers and persistence of clinical findings or culture growth despite receiving fluconazole treatment. It was accepted that candidemia eradication was not detected in at least two blood and/or catheter blood cultures. Although the patient was treated effectively and appropriately, the cause of death of the patients whose death could not be explained reason other than candidemia was accepted as *Candida* infection.

Amphotericin B was available as liposomal amphotericin B in our hospital pharmacy, so the same liposomal amphotericin B form was used in all our patients. Notification of antifungal susceptibility to our patients is at least 24 hours after the reproduction notification. Fluconazole treatment was started first in patients with *C. albicans* and when the sensitivity was announced, fluconazole was replaced with a sensitive antifungal if there was resistance. In those with *Candida* non-albicans overgrowth, empirical fluconazole, amphotericin B, or voriconazole were started, depending on the severity of the patient's disease. The treatment was readjusted when the sensitivity status was given.

All data obtained in this way was recorded in the form of patient data. The ethics committee approval was obtained by Clinical Research Ethics Committee of Harran University (decision no: 22/02/04, date: 24.01.2022) before the study began.

Statistical Analysis

Statistical analysis was performed with SPSS statistical package (IBM® SPSS® 26 SPSS Inc., Chicago, IL, ABD) for Windows 22.0. The conformity of the variables to the normal distribution was analyzed by analytical methods (Kolmogorov-Smirnov test). Descriptive analyzes were given as minimum-maximum, median and interquartile range (IQR) for continuous data. Descriptive statistics were made by giving frequency and percentage values of categorical variables belonging to sociodemographic and clinical information. Pearson's chi-square or Fisher's Exact chi-square test was used to compare the categorical variables. Significance was considered if the p-value was less than 0.05.

Results

In this study, we evaluated 27 (2.2%) patients with *Candida* species nosocomial infections in blood cultures during the stay of PICU admissions for the periods January and December 2021. The 27 (2.2%) blood cultures had candidemia, but all the *Candida* infections in this period were 75 (6.2%) which had infections like pneumonia, urinary infection, etc. The patients included in our study examined genders (girl/boy), diagnosis of hospitalizations (respiratory failure 44.4%, cardiac failure 7.4%, status epilepticus 22.2%, sepsis 3.7%, post-resuscitation 14.8%, trauma and hemolytic uremic syndrome 3.7%), and their comorbidities (congenital heart disease 7.4%, congenital metabolic disease 18.5%, cerebral palsy 44.4%, congenital anomalies 71.4%) are shown in Table 1. At the time of admission patient's age (2-204; median 55.3; IQR 90 months), length of stay (24-433; median 117.1; IQR 137 days), PRISM III score (3-98; median 98; IQR 35), at the day of the beginning of candidemia infections (9-340; median 340; IQR 85 days) and starting of antibiotics days (9-340; median 340; IQR 85 days) at the time of candidemia are shown in Table 2. At the first evaluations of patients Glasgow coma scale [GCS >8: 10 (37%), GCS <8: 17 (63%)], first admission place [emergency service 19 (70.4%), general service 5 (18.5%)], first respiratory support [oxygen support with mask 2 (7.4%), high flow nasal cannulas 2 (7.4%), non-invasive mechanical ventilation 9 (33.3%), invasive mechanical ventilation 14 (51.9%)] and after treatment of PICU status [transferred to general service 9 (33.3%), still in PICU 6 (22.2%), exitus 12 (44.4%)] detected (Table 1).

In our study, we detected a total mortality rate of 40.7%. On the other hand, 18.5% of them were caused by nosocomial candidemia. These infections were 10 (37%) CVC infections and 17 (63%) septicemias. CVC removal was performed in 10 (37%) patients during treatment, but not 14 (51.9%). Three of these patients did not have any CVC. The localization of CVCs was 18 (66.6%) jugular, 4 (14.8%) subclavian, 2 (7.4%) femoral. High comorbidity rates and

increased length of stay cause difficulties in vascular access. For this reason, in our study, we could not remove all CVCs. The TPN support rate was 10 (37%) patients.

Our nosocomial candidemia were *C. albicans* 10 (37%) and *Candida non-albicans* 17 (63%). When looking at the subtypes of *Candida* were *C. albicans* 10 (37%), *C. tropicalis* 1 (3.7%) and *C. parapsilosis* 16 (59.3%). Resistance to fluconazole treatment was 18 (66.6%). The fluconazole 8 (29.6%), amphotericin B 18 (66.7%) and voriconazole 1 (3.7%) of the patients were initiated. At this treatment time,

Table 1. The genders, diagnosis, comorbidities, and at the first evaluations of patients GCS, first admission place, first respiratory support and after treatment of PICU status

		Frequency	Percent (%)
Gender	Girl	13	48.1
	Boy	14	51.9
	Total	27	100
Diagnosis of hospitalization	Respiratory failure	12	44.4
	Cardiac failure	2	7.4
	Status epilepticus	6	22.2
	Sepsis	1	3.7
	Post-resuscitation	4	14.8
	Trauma	1	3.7
	Hemolytic uremic syndrome	1	3.7
	Total	27	100
Comorbidity	Congenital heart disease	2	7.4
	Congenital metabolic disease	3	18.5
	Cerebral palsy	7	44.4
	Congenital anomalies	8	71.4
	None	7	25.9
	Total	27	100
Glasgow coma scale	>8	10	37
	<8	17	63
	Total	27	100
First admission	Emergency service	19	70.4
	General service	5	18.5
	Other hospital	3	11.1
	Total	27	100
First respiratory support	Oxygen support with mask	2	7.4
	High flow nasal canulas	2	7.4
	Non-invasive mechanical ventilation	9	33.3
	Invasive mechanical ventilation	14	51.9
	Total	27	100
Exit from the PICU	Transferred to general service	9	33.3
	Still in PICU	6	22.2
	Exitus	12	44.4
	Total	27	100

GCS: Glasgow coma scale, PICU: pediatric intensive care unit

Table 2. At the time of admission patient's age, length of stay, PRISM III score, at the beginning of candidemia infections and use of antibiotics days at the time of candidemia

	Minimum-maximum	Median	IQR
Age (month)	2-204	55.3	90
Lenght of stay in PICU (day)	24-433	117.1	137
PRISM III score	3-98	98	35
Candidemia day	9-340	340	85
Antibiotic day	9-340	340	85

PRISM III: Pediatric Risk of Mortality, IQR: interquartile range, PICU: pediatric intensive care unit

Table 3. The evaluation of candidemia risk factors and the effectiveness of management strategy

			p-values
The effectiveness of management	Mortality	PRISM III	1.232
		Candida subtypes	0.975
		TPN using	0.070
Candidemia risk factors	TPN using	CVC/AVC infections	0.563
	Lenght of stay	Sepsis	1.060
		CVC/AVC infections	1.330

PRISM III: Pediatric Risk of Mortality, CVC/AVC: central venous catheters/arterial catheters

4 (14.8%) of patients developed organ failure. These were renal 2 (7.4%), hepatic 2 (7.4%) and coagulopathy 4 (14.8%). The rate of dialysis requirement was 4 (14%) (one of them hemodialysis and 3 peritoneal).

The mortality risk did not change for the subtypes of candidemia in our study (p=0.975). Additionally, when the patients were divided into two groups *C. albicans* (27%) and *Candida non-albicans* (63%), mortality risks did not change (p=0.916), again. No significant correlation was found when mortality (p=0.070) and CVC/AVC infection (p=0.563) were compared in patients using TPN. In our study PRISM III scores and the mortality rates of nosocomial candidemia patients were compared and no correlation was detected (p=1.232). When the length of stay was compared with catheter infection (p=1.330) and sepsis (p=1.060), no significant correlation was found. When the treatment process of our patients with exitus is examined, the statistical evaluation of the effects of PRISM III, *Candida* subtypes and TPN on this situation is given in Table 3. The statistical relationship between the use of TPN, prolonged hospital stay, the use of CVC/AVC and the occurrence of candidemia, sepsis which are among the main factors that may cause candidemia in the PICU, are also shown in Table 3.

The resistance of fluconazole was compared with hemogram (p=0.727) and arterial blood gas (p=0.348) disorders, it has not detected significant correlations. There was no organ failure during candidemia treatment time in 22 (81.5%) patients. Moreover, these patients had *C. albicans* 7 (31.8%), *C. tropicalis* 1 (4.5%), *C. parapsilosis* 14 (63.6%). When examined in terms of the development of organ failure and the duration of candidemia treatment, there was no correlation between them (p=0.441).

Discussion

Nowadays, candidemias are accepted in pediatric and adult ICUs one of the most common nosocomial infections (9). Hegazi et al. (10), conducted a study that included 589 children in a study and detected 66 (19%) candidemia. In the literature candidemia incidence is 6.4 cases/1000 (0-14.1 cases/1000 admissions) admissions. The Italian adult intensive care study reported 10.1 cases/1000 admissions and Zaoutis et al. (3) study in PICU detected candidemia in 3.5/1000 admissions (11). Invasive candidiasis is caused to be higher morbidity and mortality, especially in immunocompromised and hospitalized. In a year average of 750,000 cases are reported all around the world. The severe diseases/multiple organ failures (MOFs) are detected in invasive candidiasis developed immunocompromised children in PICU/neonatal intensive care unit. The most common isolated *Candida* subtypes are *C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, C. krusei,* etc. (12).

Candidemia usually has the same signs and symptoms as general sepsis in childhood, with a death rate of 13% (13). The most commonest pathogen in *Candidas*, in the past was *C. albicans*. Nowadays, *non-albicans Candidas* (especially *C. parapsilosis* and *C. tropicalis*) is being isolated in blood cultures more often, due to increasing resistance of antifungal treatments for *Candida* spp. in PICU (5,14). In a year our PICU admissions average of 1200 and, nosocomial candidemia rate is detected at 2.25% [*C. albicans* 10 (37%) and *non-albicans Candida* 17 (63%)] and general *Candida* infections rate is detected at 10.7% in our study time. When looking at the subtypes of *Candida* were *C. albicans* 10 (37%), *C. tropicalis* 1 (3.7%), and *C. parapsilosis* 16 (59.3%). Contrary to our study, in the study of Uysal Yazici et al. (15) evaluating candidemia cases in the PICU in our country, *C. albicans* was found to be the most common cause (45%). In the study of Ergül et al. (16) in which they evaluated candidemia cases for 3 years in the PICU, 59.1% *C. albicans,* 27.3% *C. parapsilosis*, 13% *C. tropicalis* they were found.

The study conducted by Ağın et al. (6) identified the risk factors of *Candida* infections which were an underlying disease, administration of TPN, and central venous catheterization. Immunocompromised (hematological malignancies, neutropenia, primary immune deficiency, hemopoietic stem cell or solid organ transplantation, corticosteroid treatment, etc.), gastrointestinal tract disease (malignancy, hepaticobilier diseases, etc.), ICU admissions, IV treatments (TPN, transfusion, etc.), presence of medical supports (CVC, urinary catheter, AVC, etc.), age groups (elderly, neonates, prematurity, immaturity, etc.), receipt of broad-spectrum antibiotic agent/s, trauma and burns diseases are the risk factors of invasive candidiasis (17). Different studies like this supported to understand, the timing and treatment periods of *Candida* infections (18). In our retrospective study periods, the patient's diagnoses of hospitalization in order of frequency were detected as respiratory failure (44.4%), status epilepticus (22.2%), post-resuscitation (14.8%), cardiac failure (7.4%), sepsis (3.7%), trauma (3.7%), and hemolytic uremic syndrome (3.7%). Our hospital, a tertiary PICU, is in a socioculturally underdeveloped center of a developing country. The heterogeneous population of including our study usually had comorbidity. Therefore, increased length of stay, more needed CVC, and mechanical ventilation, feeding problems to cause TPN needing have accelerated the occurrence of nosocomial *Candida* infections, sepsis and higher mortality. The mortality rate due to candidemia was detected at 44.4%, but the correlation of candidemia and mortality was not significant. Additionally, no significant correlation was found when mortality and catheter infection were compared in patients using TPN.

Repeated and prolonged use of antibiotics/antifungals due to prolonged hospitalization can be caused candidemia and resistance to antifungal agents (9,10). The age group of our patients was 55.3 (2-204; IQR: 90) months which supported their weak immunity. The average period time length of stay in PICU was 137 (24-433; IQR: 137) days and the first 24 hours calculated PRISM III score was 98 (3-98; IQR: 35). These highest PRISM III scores and at the time of admission severe respiratory support needing could be caused high nosocomial infections and candidemia (8). Although these high risks of candidemia, length of stay and PRISM III were compared with nosocomial candidemia, we did not detect any correlation. When examined for candidemia day 340 (9-340; IQR: 85) had a high antibiotics day 340 (9-340; IQR: 85) was detected. Therefore, the resistance to fluconazole treatment was 18 (66.6%) patients. The fluconazole 8 (29.6%), amphotericin B 18 (66.7%) and voriconazole 1 (3.7%) of the patients were initiated. All the candidemias were examined, CVC nosocomial *Candida* infections rate was detected in 15 (55.5%) patients and this group treatment success was 12 (80%) patients, but unfortunately 3 (20%) patients died because of CVC infection. Similarly, Ağın et al. (6) in a study in our country investigating the risk factors for *Candida* infections in PICU, the rate of *Candida*-associated catheter infection was found to be 59.6%. Only 5 (18.5%) patients developed any organ failure. If examined in terms of the development of organ failure and the duration of candidemia treatment, there was no correlation between them. Non-immunocompromised patients have candidemia of severe sepsis/septic shock is very rare. Additionally, if septic shock develops, it is caused a high mortality rate because of MOF. Not only does candidemia cause MOF, using antifungal agents for a long time and/or strong agents causes, too (19).

The presence of CVC increased candidemia three times was reported (20). Especially *C. parapsilosis* was produced spread biofilm areas on central venous lines and then associated with nosocomial candidiasis. Also, *C. parapsilosis* colonization on hands was detected (21).

Our nosocomial candidemia were *C. albicans* 10 (37%) and *Candida non-albicans* 17 (63%). When looking at the subtypes of *Candida* were *C. albicans* 10 (37%), *C. tropicalis* 1 (3.7%) and *C. parapsilosis* 16 (59.3%). The mortality risk did not change for the subtypes of candidemia in our study. Additionally, when the patients were divided into two groups *C. albicans* (27%) and *Candida non-albicans* (63%), mortality risks did not change, again. In the study of Uysal Yazici et al. (15), the mortality rate in candidemia cases was found to be 35%, which is lower than in our study. Again, in this study, while mortality was 44.4% in cases with *C. albicans* overgrowth, it was 36.4% in *non-albicans Candida*. No statistically significant difference was found between the *Candida* subtype and mortality rates (15). Till today all studies suggested removing the CVC if catheter infections. Unless you must use CVC, it must be removed CVC for treatment of resistant infection and/or uncontrolled infection (22). The localization of CVCs was 18 (66.6%) jugular, 4 (14.8%) subclavian, 2 (7.4%) femoral. Since the socioeconomic status is low in the region where our hospital is located, malnutrition, multiple genetic anomalies, and long hospital stays are very common. For all these reasons, as the problem of finding vascular access is high, it is not possible to remove as much CVC as desired. Also, no key treatment was applied to our patients. For this reason, in our study, we could not remove all CVCs. The removal of CVC was at 10 (37%) patients for source control, but 14 (51.8%) were not removed and 3 (11.1%) were no CVC. This situation, long treatment periods, increased resistance to antifungals, morbidity, and mortality can be caused.

Multiple pharmacotherapeutic options are available for the treatments of candidemia triazoles, amphotericin B and echinocandins (23). If the effective and rapidly of appropriate antifungals are not initiated, especially pediatric patients have a high range (7.7-26%) of mortality risk (24,25). At the time of choosing antifungal treatment strategy, it is suggested for adult guidelines procedures. The rapid initiation of antifungal agents at first, than removing CVC, source control, if necessary, addition of secondary drugs, continuing treatment same agents for 14 days after blood culture without *Candida* are the basic rules (26). In our study, we applied these principles, and the fluconazole 8 (29.6%), amphotericin B 18 (66.7%), and voriconazole 1 (3.7%) of the patients were initiated. Resistance to fluconazole treatment was 18 (66.6%) who had secondary antifungal agents such as amphotericin B, caspofungin, and voriconazole. The finishing of treatment was supplied with detecting blood cultures without *Candida*. Although there has been an increase in treatment options for invasive fungal infections in recent years, use in childhood is generally limited to amphotericin B and liposomal amphotericin B preparations. There is not enough experience in the use of voriconazole from the new azole group treatments or caspofungin from the new candins in childhood (27). Although we have a tertiary and large-capacity PICU, they were not used in our study since there are no echinocandin-type antifungals (such as caspofungin, anidulafungin, etc.) in our hospital. In addition, considering current literature data as a first-line treatment choice for candidemia is reported that to used fluconazole and liposomal amphotericin B same equal in both neonates and children, except for non-neutropenic non-critically ill children (28).

The limitations are that it was retrospective, the number of patients was small, it covered a short period time, it was a single center, and the patients were heterogeneous. In addition, there were no pediatric hematology-oncology or pediatric immunology physicians in our hospital during part of the study period. Also, since there is no chemotherapy preparation unit in our hospital, patients cannot be followed up during active malignancy. For all these reasons, the immunosuppressed patient group, which is one of the riskiest groups for invasive fungal infection, was not included in our study. However, there is insufficient data on the causes, prevention, treatment and follow-up of candidemias in the critically ill group in the PICU, and we think that we will contribute to the literature.

Conclusion

In conclusion, we described *Candida* infections, management, morbidity, mortality in critically pediatric patients and evaluate the risk factors and effects of nosocomial candidiasis in a tertiary level hospital in PICU. In a single center experience: in 52-bed tertiary hospital had been evaluated treatment success and early detection of clinical signs and symptoms. A large heterogenous population of our patients had severe comorbidity and *Candida* risk factors, at the time of treatment had complications because of pathogens and/or pharmacotherapy. We aimed that, our experience with a large population of PICU admissions to

be contributed to the literature. We believe that with the contribution of our experience with nosocomial *Candida* infection in this study in the PICU, more effective treatment methods with less side-effect profile will be developed for candidemia in the future.

Ethics

Ethics Committee Approval: The ethics committee approval for the study was obtained by Harran University Clinical Research Ethics Committee (decision no: 22/02/04, date: 24.01.2022) before the study began.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.F.A., Concept: H.F.A., Design: H.F.A., Data Collection and Process: M.A., Analysis or Interpretation: M.A., Literature Search: H.F.A., M.A., Writing: H.F.A., M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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